ORYZON receives the INNOVATIVE SME seal from the Spanish Ministry of Science and Innovation

- **Innovation present in Oryzon's programs in the field of epigenetics acknowledged**
- **Oryzon currently has 2 compounds in Phase II clinical studies, iadademstat and vafidemstat**

MADRID, SPAIN and BOSTON, MA, UNITED STATES, April 4th, 2024 - Oryzon Genomics, S.A. (ISIN Code: ES0167733015, ORY), a clinical-stage biopharmaceutical company leveraging epigenetics to develop therapies in diseases with strong unmet medical need, announces that it has obtained the INNOVATIVE SME seal from the Spanish Ministry of Science and Innovation, and has consequently been registered in the Public Registry of INNOVATIVE SMEs.

By awarding this distinction, which aims to reward and highlight the R&D activities of SMEs, the Ministry formally acknowledges the innovative and pioneering nature of Oryzon's studies and clinical advances in the field of epigenetics. This is the third consecutive time that Oryzon receives the INNOVATIVE SME.

Oryzon is pioneering the development of LSD1 inhibitors in the field of psychiatric and neurodegenerative diseases. Vafidemstat is a Phase II LSD1 inhibitor, which has shown a good safety profile in clinical trials, with over 400 subjects treated, and has been shown to be effective in reducing agitation and aggression in Phase IIa clinical studies in patients with borderline personality disorder (BPD), attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and Alzheimer's disease. Vafidemstat is currently in clinical development in BPD, having recently completed the Phase IIb PORTICO trial, which has enrolled 210 patients in the US and Europe, and in schizophrenia, with the Phase IIb EVOLUTION trial, actively recruiting patients in Spain. The company presented positive and promising data from PORTICO on secondary endpoints reflecting clinically relevant improvements in overall BPD severity and agitation/aggressivity in the Top Line results presented at the JPMorgan-week in San Francisco and is currently finalizing in a satisfactory manner the analysis of the full study data. Based on the promising efficacy and safety results obtained in PORTICO, Oryzon is planning to request an end-of-Phase II meeting with the FDA to discuss plans for a registrational Phase III trial in BPD. The company plans to present final PORTICO data at a psychiatric conference later this year.

Oryzon is also pioneering the field of CNS precision medicine, where it plans to explore vafidemstat as a potential treatment for certain diseases harboring mutations in certain genes that have been shown to be amenable to treatment with LSD1 inhibitors, such as Kabuki syndrome.

Currently, Oryzon has an ongoing clinical trial (FRIDA study) of iadademstat in combination with gilteritinib in patients with relapsed/refractory (R/R) acute myeloid leukemia (AML) harboring an FMS-type tyrosine kinase mutation (FLT3mut+). Iadademstat is an orally active small molecule that acts as a potent and selective inhibitor of the epigenetic enzyme LSD1 (Lysine Specific Demethylase-1), and is the most potent compound among the LSD1 inhibitors in clinical development. The first cohort of the FRIDA study (six patients) has been completed, and the combination was safe and showed strong anti-leukemic activity. Recruitment of the second cohort (six patients) has been completed and is ongoing, and the company plans to present preliminary results from FRIDA at the next European Hematology Association congress, EHA-2024, in June in Madrid.

Beyond AML, Oryzon is also developing iadademstat for the treatment of small cell lung cancer (SCLC). Iadademstat will be evaluated in a new clinical trial in preparation in combination with an immune checkpoint inhibitor (ICI) in patients with first-line metastatic SCLC, which will be conducted under a Cooperative Research and Development Agreement (CRADA) signed with the US National Cancer Institute (NCI) and led by Memorial Sloan Kettering Cancer Center (MSKCC). Iadademstat is also being evaluated in a collaborative Phase II clinical trial with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in platinum R/R SCLC and high-grade extrapulmonary neuroendocrine tumors.

About Oryzon

Founded in 2000 in Barcelona, Spain, Oryzon (ISIN Code: ES0167733015) is a clinical stage biopharmaceutical company and the European leader in epigenetics, with a strong focus on personalized medicine in CNS disorders and oncology. Oryzon's team is composed of highly qualified professionals from the pharma industry located in Barcelona, Boston, and San Diego. Oryzon has an advanced clinical portfolio with two LSD1 inhibitors, vafidemstat in CNS and iadademstat in oncology, in several Phase II clinical trials. The company has other pipeline assets directed against other epigenetic targets like HDAC-6, where ORY-4001 has been nominated as clinical candidate for the treatment of certain neurological disorders such as CMT and ALS. In addition, Oryzon has a strong platform for biomarker identification and target validation for a variety of malignant and neurological diseases. For more information, visit www.oryzon.com

About Iadademstat

Iadademstat (ORY-1001) is a small oral molecule, which acts as a highly selective inhibitor of the epigenetic enzyme LSD1 and has a powerful differentiating effect in hematologic cancers (see Maes et al., Cancer Cell 2018 Mar 12; 33 (3): 495-511.e12.doi: 10.1016 / j.ccell.2018.02.002.). A FiM Phase I/IIa clinical trial with iadademstat in R/R AML patients demonstrated the safety and good tolerability of the drug and preliminary signs of antileukemic activity, including a CRi (see Salamero et al, J Clin Oncol, 2020, 38(36): 4260-4273. doi: 10.1200/JCO.19.03250). Iadademstat has shown encouraging safety and efficacy data in combination with azacitidine in a Phase IIa trial in elder 1L AML patients (ALICE trial) (see Salamero et al., ASH 2022 oral presentation). Iadademstat is currently being evaluated in combination with gilteritinib in the ongoing Phase Ib FRIDA trial in patients with relapsed/refractory AML with FLT3 mutations. Beyond hematological cancers, the inhibition of LSD1 has been proposed as a valid therapeutic approach in some solid tumors such as small cell lung cancer (SCLC), neuroendocrine tumors (NET), medulloblastoma and others. In a Phase IIa trial in combination with platinum/etoposide in second line ED-SCLC patients (CLEPSIDRA trial), preliminary activity and safety results have been reported (see Navarro et al., ESMO 2018 poster). Iadademstat is being evaluated in a collaborative Phase II basket study with the Fox Chase Cancer Center (FCCC) in combination with paclitaxel in R/R neuroendocrine carcinomas, and the company is preparing a new trial in combination with immune checkpoint inhibitors (ICI) in SCLC. Oryzon has entered into a Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute (NCI) to collaborate on potential further clinical development of iadademstat in different types of solid and hematological cancers; a first trial in combination with ICI in SCLC is under preparation. In total iadademstat has been dosed so far to more than 130 cancer patients in four clinical trials. Iadademstat has orphan drug designation for SCLC in the US and for AML in the US and EU.

About Vafidemstat

Vafidemstat (ORY-2001) is an oral, CNS-optimized LSD1 inhibitor. The molecule acts on several levels: it reduces cognitive impairment, including memory loss and neuroinflammation, and at the same time has neuroprotective effects. In animal studies vafidemstat not only restores memory but reduces the exacerbated aggressiveness of SAMP8 mice, a model for accelerated aging and Alzheimer's disease (AD), to normal levels and also reduces social avoidance and enhances sociability in murine models. In addition, vafidemstat exhibits fast, strong, and durable efficacy in several preclinical models of multiple sclerosis (MS). Oryzon

has performed two Phase IIa clinical trials in aggressiveness in patients with different psychiatric disorders (REIMAGINE) and in aggressive/agitated patients with moderate or severe AD (REIMAGINE-AD), with positive clinical results reported in both. Additional finalized Phase IIa clinical trials with vafidemstat include the ETHERAL trial in patients with Mild to Moderate AD, where a significant reduction of the inflammatory biomarker YKL40 has been observed after 6 and 12 months of treatment, and the pilot, small-scale SATEEN trial in Relapse-Remitting and Secondary Progressive MS, where anti-inflammatory activity has also been observed. Vafidemstat has also been tested in a Phase II in severe Covid-19 patients (ESCAPE) assessing the capability of the drug to prevent ARDS, one of the most severe complications of the viral infection, where it showed significant anti-inflammatory effects in severe Covid-19 patients. Vafidemstat is being investigated in neuropsychiatric disorders in two double-blind, randomized, placebo-controlled Phase IIb trials: one in schizophrenia, named EVOLUTION (recruitment ongoing), and another one in Borderline Personality disorder (BPD), named PORTICO, recently finalized, with topline data and in the process of completing the full data analysis. Based on PORTICO's topline results, the company is planning to request an End-of-Phase II meeting with the FDA to discuss options for a registrational Phase III trial in BPD. The company is also deploying a CNS precision medicine approach with vafidemstat in genetically-defined patient subpopulations of certain CNS disorders and is preparing a clinical trial in Kabuki Syndrome patients. The company is also exploring the clinical development of vafidemstat in other neurodevelopmental syndromes.

FORWARD-LOOKING STATEMENTS

This communication contains, or may contain, forward-looking information and statements about Oryzon, including financial projections and estimates and their underlying assumptions, statements regarding plans, objectives, and expectations with respect to future operations, capital expenditures, synergies, products and services, and statements regarding future performance. Forward-looking statements are statements that are not historical facts and are generally identified by the words "expects," "anticipates," "believes," "intends," "estimates" and similar expressions. Although Oryzon believes that the expectations reflected in such forward-looking statements are reasonable, investors and holders of Oryzon shares are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Oryzon that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include those discussed or identified in the documents sent by Oryzon to the Spanish *Comisión Nacional del Mercado de Valores* (CNMV), which are accessible to the public. Forward-looking statements are not guarantees of future performance and have not been reviewed by the auditors of Oryzon. You are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date they were made. All subsequent oral or written forward-looking statements attributable to Oryzon or any of its members, directors, officers, employees, or any persons acting on its behalf are expressly qualified in their entirety by the cautionary statement above. All forward-looking statements included herein are based on information available to Oryzon on the date hereof. Except as required by applicable law, Oryzon does not undertake any obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise. This press release is not an offer of securities for sale in the United States or any other jurisdiction. Oryzon's securities may not be offered or sold in the United States absent registration or an exemption from registration. Any public offering of Oryzon's securities to be made in the United States will be made by means of a prospectus that may be obtained from Oryzon or the selling security holder, as applicable, that will contain detailed information about Oryzon and management, as well as financial statements.

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